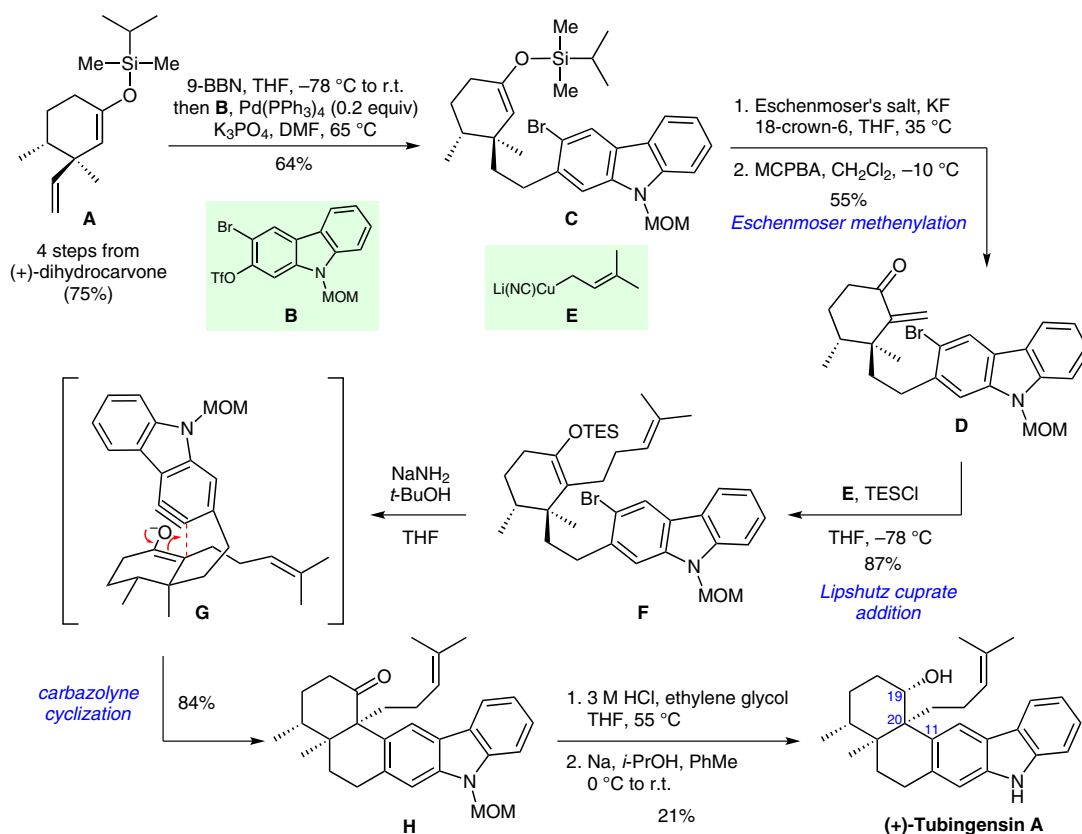


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Total Synthesis of (+)-Tubingensin A



Significance: The alkaloid (+)-tubingensin A, isolated in 1989 from the fungus *Aspergillus tubingensis*, possesses a wide array of biological activity against cancer, viruses, and insects. Structurally, this natural product is characterized by a substituted *cis*-decalin which is attached to a carbazolyne unit. Given their interest in coupling reactions between electrophilic heteroarynes and enolates (see for example: *Org. Lett.* **2009**, *11*, 2349), Garg and co-workers focused on the key C–C bond formation between C11 and C20.

Comment: The total synthesis of the target compound started with hydroboration of **A** and subsequent alkyl Suzuki cross-coupling with triflate **B**. The aliphatic side chain was introduced by an Eschenmoser methenylation followed by Lipshutz cuprate addition to yield key intermediate **F**. Exposing **F** to sodium amide and *tert*-butanol generated both the carbazolyne and the enolate, which cyclized in remarkable 84% yield to ketone **H**. Although deprotection at the nitrogen proceeded smoothly, the diastereoselective reduction of the ketone proved to be challenging. While several standard reduction protocols gave unsatisfying results, sodium and isopropanol provided (+)-tubingensin A in 4% overall yield.